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MALIGNANT TUMORS OF THE SMALL AND LARGE INTESTINES IN INFANTS AND CHILDREN

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Malignancy of the intestinal tract, though common in adults, is rare in children. Nevertheless, a sufficient number of cases have been reported in the literature to justify closer scrutiny of the problem. The youth of a patient suffering symptoms of intestinal dysfunction has miliated against a diagnosis of malignancy because it has always been taught that the 40-60 age group is the vulnerable group. Though this is undoubtedly true, little or no mention is made of the consideration of malignancy in the young, as far as the intestinal tract is concerned, in many papers and textbooks. For this reason, the mortality in malignancy occurring in children has been exceptionally high. Whereas in adults, malignancy of the intestine is readily considered in any protracted or obscure intestinal complaint, it is very rarely considered, under the same conditions, in a young individual. If it was considered as a diagnostic possibility more frequently it would certainly minimize the great percentage of cases diagnosed only in the operating room or on the autopsy table.

It is with this purpose in mind, that I have collected every available case reported in the literature, of sarcoma and carcinoma of the small and large intestine in young individuals between 0-19 years of age. This series includes 142 cases of carcinoma and 76 cases of sarcoma.

SARCOMA OF THE SMALL AND LARGE INTESTINE

Cameron[7] states that 10% of the cases of sarcoma of the small intestine occur in infants and children. This compares with the findings of those authors, who have collected large series of cases, among them Baltzer (75 cases), Libman[27] (59 cases), Crowther (191 cases), Graves (249 cases), Ullman and Abeshouse[54] (126 cases), Sugarbaker and Craver[53] (196 cases), and others. Rankin[44] believes it is a disease of early youth and young adult life. Most cases are found in the first, third, and fourth decades. Though a rare condition, Simpson-Smith[48] collected 106 cases in children from 1852-1938. He found that the greatest incidence is in children between the ages of one and five. In the 76 cases reviewed, 17 cases occurred in the first five years of life, the youngest being the case reported by Stern in 1909, in which the child had a palpable abdominal tumor at birth and died five days later of intestinal obstruction. Pathological examination revealed the mass to be angiosarcoma of the jejunum. The oldest cases in this series are eighteen years of age.

Males are affected two to three times more often than females. Simpson

Smith[48] found a proportion of 3:1 in favor of males, which agrees with the findings of most authors. In this series there were 24 males and 6 females, with 46 cases in which sex was not specified.

Duodenum	2	
Jejunum	2	
Ileum	59	(77.6%)
Ileo-cecum	2	
Cecum	3	
Ascending Colon	2	
Sigmoid	1	
Rectum	4	
Large int. (?)	1	
	76	

Chart 1—Distribution of cases

The etiology is unknown, but among the theories proposed are that of trauma or abdominal contusion advanced by Boyce and McFetridge and Ullman and Abeshouse. Though there is a history of trauma preceeding the tumor in some cases, there is no proof that the trauma is the cause of the growth.

The pathologic varieties are many. Raiford[43] divides them into: lymphosarcoma, reticulum cell sarcoma, endothelioma, fibrosarcoma, myosarcoma, neurofibrosarcoma, and non-specific granulomas. The most common type is the lymphosarcoma or lymphoblastoma. In this series 93.4% were lymphosarcomas (chart 2). Since the parenchymal cells are lymphoblasts or lymphocytes, lymphosarcomas are far more common in the distal ileum, as might be expected, due to the preponderance of lymphoid tissue in that part of the intestinal tract. The growth is usually primary in the intestine and tends to remain localized to that section of bowel or to the bowel and adjacent nodes. Only $\frac{1}{12}$ of the cases exhibit plural sites of origin according to Cameron[7]. If the tumor arises elsewhere and spreads to the bowel, it gives rise to extensive sarcomatosis. The mass is usually soft and friable and the bulk of the tumor is in the mucosa and submucosa, sometimes encroaching on the lumen in tube-like fashion. Ulceration is frequent, as is the presence of nodules on the serosa with adhesions between adjacent loops of bowel. Metastases occur in about 50% of the cases to the regional and distant lymph nodes.

Lymphosarcoma	71	(93.4%)
Recticulum Cell Sarcoma	2	
Angiosarcoma	1	
Spindle Cell Sarcoma	1	
Unspecified	1	
	76	

Chart 2—Pathological type of Sarcoma in a total of 76 reported cases

As was mentioned above, the ileum is the site of predilection, with the jejunum and cecum being next in order of frequency. In this series 84.2% occurred in the small intestine, and of these, 77.6% were in the ileum. Due to the narrow diameter of the small intestine, sarcomas usually obstruct the gut in the form of annular masses, by intussusception, by encroachment on the lumen from inside, by compression from the outside, or by angulation of the bowel wall as a result of adhesions between its coils.

The symptomatology varies with the location and size of the tumor. The majority of cases however, present either the picture of an acute abdomen or of progressive constitutional symptoms with loss of weight, strength and anemia. Acute intestinal obstruction may be the first indication that there is any intestinal pathology. In Simpson-Smith's series of 106 cases in children, 24% developed intussusception and 63% presented a palpable tumor. A mass which is felt at one examination and absent at the next should suggest a tumor of the small intestine, since with change in position and posture, that loop of freely movable small gut may very easily escape detection. Regardless of whether or not a tumor mass is palpable, the usual complaints are griping abdominal pains with or without vomiting, constipation or diarrhea, and at times fever. It may simulate an acute appendicitis but the pain does not usually tend to localize in one spot. Frequently occult blood is found in the stools (with patient on meat-free diet). This finding is very important since it indicates a bleeding lesion somewhere in the intestinal tract. With this aid, the lesion may be localized by X-ray studies.

Illness, pallor, wasting, vomiting, or occult blood in the stools, occurring in a child without an obvious cause, should suggest sarcoma of the intestine. If, as is rarely the case, the growth is in the duodenum, colon, or rectum, particular evidence of its presence may be found. Vomiting of bile or vomiting and jaundice with gastric distention should suggest a duodenal tumor, whereas low intestinal obstruction with distention and colicky pains should suggest a tumor of the large intestine. Rectal sarcomas are rare. They may manifest themselves either by bleeding per rectum, pruritus ani, constipation or change in the bowel habits, or by presenting a mass which is palpable on rectal examination. Thus depending on the location of the tumor, the symptoms vary. In general, however, griping abdominal pain, vomiting, loss of weight and strength, and anemia are the common findings.

The diagnosis can be suspected from the history and afore-mentioned findings, and in many cases proven by either a flat plate of the abdomen, in which the small gut is seen to be greatly distended with gas, or by barium with air contrast, in which the defect or obstructive lesion can be visualized.

The course of the disease, with particular reference to the lymphosarcomas, depends on several factors which, according to Stout[52] are: (1) in-

dividual inherent qualities for growth and dissemination of the tumor; (2) the extent of the disease on admission; (3) the location of the lesion; (4) the complication of leukemia and pseudoleukemia; (5) the age of the patient—the younger the patient the less the chances of survival. The early diagnosis is by far the most important factor, as is true in any malignancy anywhere in the body. To diagnose it, it must be suspected and to suspect it, one must know that the condition exists. The majority reported were fatal, with courses ranging from 5 days to 3 years, the average being 6 months. In Simpson-Smith's series, 60% died within 6 months of diagnosis and 92% within 12 months of diagnosis. The longest recorded survival is the case of a seven year old boy reported by Charache[9], in which the patient is well nine years after operation for a lymphosarcoma of the ileum. During that interval the patient was closely followed at the Brooklyn Cancer Institute.

The treatment is unsatisfactory because most of the cases are too far-gone when operated on. However, if the tumor is localized and metastases have not occurred, surgical removal with resection of the bowel is curative. Preoperative X-ray therapy, followed by surgery and post-operative radiation, seems to be the treatment of choice.

CARCINOMA OF THE INTESTINAL TRACT

Though supposedly rarer in the young than sarcoma, there were 142 cases of carcinoma of the intestinal tract found in the literature. This can best be explained by the fact that cases of carcinoma are, for the most part, reported individually, or if reported in reviews, the names of the authors are given. The sarcoma studies are reported in the majority of cases generally without reference to the source of the cases, and for this reason an accurate review was impossible. Simpson-Smith[48], though reporting 106 cases of intestinal tract sarcoma, gives no particulars about individual cases; so to prevent probable overlapping his series was of necessity excluded. The author did not find this difficulty in reviewing cases of carcinoma which may possibly explain the more complete nature of this portion of the study.

Cancer in childhood involves certain organs far more often than the intestinal tract, as can be gathered from the great number of ovary, liver, and skin cases and the relatively few intestinal cases. Ritvo[45], in a study of 72 cases of childhood cancer from the records of the Boston City Hospital, found only one intestinal cancer, that being an adenocarcinoma of the descending colon in a fifteen year old girl. Sittenfield[49], in a discussion of cancer in the young, makes no mention of the gastro-intestinal tract save to say that Ullhorn gathered 69 cases of rectal cancer in children under fifteen. Yet carcinomas carry such a grave prognosis, particularly in the

young, that they deserve an important place in the differential diagnosis of intestinal complaints.

Duodenum	6 (4.2%)
Jejunum	6 (4.2%)
Cecum	7 (4.9%)
Ascending Colon	7 (4.9%)
Transverse Colon	4 (3.8)
Splenic Flexure	6 (4.2%)
Descending Colon	3 (2.1%)
Sigmoid Colon	20 (14%)
Recto-sigmoid	12 (8.4%)
Rectum	70 (49.3%)
Unclassified	1
	142

CHART 3—DISTRIBUTION OF 142 CASES OF CARCINOMA OF THE BOWEL REPORTED IN CHILDREN

a) *Small intestine.* Carcinoma of the small bowel is rare. Only 8.4% of the 142 cases reviewed in this series occurred in the small intestine (chart 3). Sarcoma, quite to the contrary, is very prominent in that part of the bowel. While in sarcoma the ileum is the site of predilection, in carcinoma the duodenum predominates and constitutes roughly 70-75% of small gut cancers. Because of this fact, it is proper that a discussion of small intestine cancer be essentially one of cancer of the duodenum.

There have been, and still are, many theories advanced on the etiology of duodenal carcinoma. Among the most prominent is the one postulating irritation by the alkaline juices from the pancreatic and biliary duct systems and the acid gastric contents. There are many others, including those which, (1) advance supervention on chronic duodenal ulcer (extremely rare in children); (2) believe that malignant degeneration of a previously benign lesion such as a polyp or papilloma occurs; (3) claim origin in aberrant gastric glands, pancreatic, or thyroid tissue; (4) believe there is a transition of the junctional epithelium at the termination of the ducts. Suffice it to say that irritation seems somewhat more likely since there has been considerable evidence pointing to that mechanism in many other organs such as cancer of the cervix, skin, and tongue. However, proof is still forthcoming. The fact that roughly two-thirds of duodenal cancers occur in its second part or ampullary portion favors this theory somewhat since the ducts empty into that portion. The first part of the duodenum is the site next in order of frequency, with the third part least affected.

In a review of 222 cases collected by Lieber[28], the age varied from 15-82, with the greatest number occurring in the fifth and sixth decades of life. In addition to Lieber's case in a 15 year old male, Whittier reported 3 cases,

Ewald reported 1, and Hoffman-Pack 1, a total of 6 in young individuals below twenty years of age. Males predominated 3:1.

Carcinoma of the duodenum, according to Lieber[28], may involve: (1) the ampulla of Vater; (2) the terminal duct of Wirsung; (3) the terminal common bile duct; (4) the intestinal mucous membrane covering the papilla of Vater; (5) all the epithelial structures of the papilla of Vater; (6) all the papillary structures exclusive of the mucous membrane covering it. The usual type is a glandular cancer from the duodenal mucous membrane consisting of cylindrical cells. It may be scirrhous with few cells and abundant fibrous tissue stroma, a soft and bulky polypoid mass with ulceration and necrosis, or a colloid type with mucoid degenerative changes.

The symptoms and signs vary according to the structures involved, so that cancer of the duodenum is usually classified clinically as supra-papillary, papillary, and infra-papillary depending on whether the involvement is above, at or below the papilla of Vater.

The onset is relatively acute and ushered in by signs and symptoms of obstruction of the duodenum or its neighboring structures. When the obstruction is above the papilla, the early symptoms are loss of appetite, epigastric distention and fullness, nausea, and eructation. Later, epigastric pain, vomiting, dehydration, constipation and loss of weight and strength make their appearance. Visible peristaltic waves may occasionally be seen running across the upper abdomen and a mass may be felt in the epigastrium in one-third of the cases. The vomitus contains undigested food particles from previous meals, indicating gastric retention. As a rule, the vomitus will be free of bile if the obstruction is complete. It simulates pyloric stenosis with the exception that the appetite is diminished.

Obstruction at the papillary region is more dramatic and acute in onset. The patient becomes increasingly and progressively jaundiced. In Lieber's[28] series, all but 4 of the 222 cases exhibited jaundice. It is deep and painless (50% of the cases) and in this respect resembles carcinoma of the head of the pancreas. Differentiation from the latter condition is often difficult. Vomiting occurs in about 30% of the cases at some time. The gall-bladder is commonly distended and palpable (Courvoisier's Law), and the liver is palpable in most cases. The urine contains bile but is devoid of urobilinogen since bile does not gain access to the intestinal tract and therefore cannot be reduced. The stools are usually light or clay-colored and may contain blood if ulceration occurs. If the pancreatic duct is occluded, the stools may exhibit a greasy appearance and reveal undigested muscle fibers, increased neutral fat, and increased total nitrogen. Further evidence of pancreatic duct occlusion is afforded by drainage of the duodenum and assay of the recovered juice for pancreatic ferments.

The infrapapillary type gives the picture of high intestinal obstruction

with cramping abdominal pain, vomiting and a palpable tumor mass proximal to the ligament of Treitz. The vomitus contains bile and pancreatic juice, and the stools are decreased in amount and dark, giving them the appearance of starvation stools. If there is ulceration of the tumor, the stools will reveal gross or occult blood.

The X-ray is of great value in the diagnosis of duodenal cancers, as is pointed out by Weintraub and Tuggle[59] who state that one or several of the following signs is seen on the X-ray: (1) obstruction of some portion of the duodenum; (2) filling defect of the duodenum; (3) disturbances of the mucosal pattern; (4) pressure defects of the bulb; (5) distortion of the normal duodenal swing; (6) pressure defects on the greater curvature of the antrum; (7) air in the bile ducts.

The course is steady and progressive, but due to the rapidity with which obstruction of the duodenum itself or its structures occurs, attention is quickly called to the condition and operation performed. For this reason, metastases are not commonly seen. The treatment is surgical, and if instituted early in the course of the disease, life may be prolonged and at times the condition cured. Of 122 cases in Lieber's series which were operated on, the average life was two years from the onset of symptoms, as compared with an average life of 6.63 months in those cases not treated surgically.

Carcinoma of the jejunum is rare due to the alkaline reaction therein, the fluid nature of the contents, and the lack of stasis in this part of the small bowel. Six cases were found in the literature, the youngest being that of a $3\frac{1}{2}$ year old male reported by Duncan in 1886, in which the first sign of pathology was perforation of the bowel. The usual findings are those of acute high intestinal obstruction.

Carcinoma of the ileum, in direct contrast to sarcoma, is almost unheard of. A careful review of the literature failed to reveal any cases in children. Its manifestations however, are those of obstruction, weight loss, bleeding, and anemia.

LARGE INTESTINE

Cancer of the colon and rectum ranks first among digestive tract malignancy. In this series 91.5% of the 142 cases occurred in the large intestine. The youngest case was that reported by Ahfeld in 1880 of a newborn monster with a carcinoma of the sigmoid, and the oldest cases were nineteen years of age. The majority of cases occurred between the ages of 11–19 (126). Of these, 79 were in the 11–15 age group. Males predominated slightly more than 2:1 with 71 males and 32 females. In 39 cases no sex was specified.

The etiology of colonic cancer is unknown, but many precancerous lesions

are recognized and known to develop into cancer if left in long enough. Among these are polyps, inflammatory lesions, and adenomas. Polyps may be single, multiple, or diffuse. According to Abell[1] it is the most frequent precancerous lesion noted in the colon and rectum. Ulcerative colitis, in which constant destruction and repair occurs, may result in carcinoma not infrequently in the young when the repair stage of the disease runs rampant. These two conditions occur in young people more often than in adults because diffuse polyposis is frequently familial and because ulcerative colitis is a disease of the young.

The lower colon, from the descending colon to the rectum, comprises roughly 75% of the cases with the rectum the most frequent site. Of the 142 cases analyzed 49.3% were in the rectum while 73.8% occurred in that part of the large bowel extending from the descending colon to and including the rectum. This finding compares with other reports.

The growth may be grossly classified as: (1) projecting or polypoid; (2) infiltrating and ulcerative; and (3) stenosing. Microscopically they are classified as adenocarcinoma, scirrhous carcinoma, and colloid carcinoma depending on the character of the cells.

In order to facilitate reading, and because of the characteristic clinical picture presented by cancers at different levels of the large intestine, it will be discussed under the headings of cancer of the right half, left half, and rectum.

RIGHT HALF OF THE COLON

This section of the colon includes the cecum, ascending colon, hepatic flexure, and the proximal one-half of the transverse colon. Eighteen cases at these levels are reported in the literature, seven being in the cecum, seven in the ascending colon, and four in the transverse colon. The age varied from 5 to 19 with males predominating 3:1.

The function and anatomy of the right half of the colon is responsible for the difference in the clinical picture it presents from lesions of the left half of the colon. First, this part of the colon is greater in diameter; second, the contents are liquid in nature; and third, it is fixed and allows palpation more readily. For these reasons lesions here are characterized by their ability to produce profound anemia. The growth rarely obstructs the bowel, but rather ulcerates and bleeds, so that frequently the only manifestation is unexplained secondary anemia. Due to the fixed nature of the right colon, a mass is frequently palpable. Pain too is a common finding, and in many cases resembles the syndrome of appendicitis with right lower quadrant pain and tenderness. Wakely and Rutherford[55] state that 50% of cecal cancers have leukocytosis which further enhances the probability of that diagnosis. However, careful study will usually reveal tarry stools,

or at least occult blood in the stools, depending on the degree of ulceration. Characteristically, abdominal pain particularly on the right side, a palpable mass, and anemia are present. Priestly and Bargen[12], in reviewing 100 cases of carcinoma of the transverse colon, found that pain was by far the most frequent initial symptom. It is described as intermittent and colicky, occurring after meals, and relieved by the passage of a stool or gas. Vomiting accompanies the more severe attacks and gives the picture of partial intestinal obstruction. Gradually increasing constipation was next in order of frequency, with loss of weight, palpable mass, and bloody stools less frequently seen. In the case reported by Warthen[56], the patient, a 14 year old female, complained of colicky upper abdominal pains and constipation. On examination a large midline mass was palpated. In many cases however, a mass is not palpated.

LEFT HALF OF THE COLON

This level of the colon from the distal half of the transverse colon to and including the sigmoid has for its function the storage of feces which are less liquid in consistency than the contents of the right half. Also, the lumen is smaller. For these reasons mechanical obstruction is far more common and anemia less common. Pain is the earliest symptom and is usually generalized over the entire abdomen. Sooner or later acute ileus occurs and symptoms and signs of low intestinal obstruction with recurrent colicky abdominal pain, distention and increased peristalsis make their appearance. The early symptoms however, are increasing constipation alternating at times with diarrhea, pain, and rectal bleeding. Since the bleeding is lower down in the bowel, the stools usually contain fresh blood or clots.

RECTO-SIGMOID AND RECTUM

In the young the rectal region is more adapted as a region where intestinal contents stagnate than other portions of the intestine, and it is on this basis that it is believed cancer here is more common due to irritation by fecal material. In this report 12 recto-sigmoid and 70 rectal carcinomas are recorded. Of these, 7 occurred in the 0–10 age group, 48 in the 11–15 age group, and 27 in the 16–19 group. Males predominated roughly 2:1. The youngest case is one reported by Mayo and Madding[33] of a $2\frac{1}{2}$ year old child with adenocarcinoma of the rectum.

Rectal cancers tend to be quite silent early. However, routine digital examination of the rectum will undoubtedly help discover early cases since at least one-third of the cancers of the large intestine are in the rectum, within easy reach of the finger. The diagnosis was made by digital and proctoscopic examination alone in 100% of the cases reported by Mayo and Madding[33].

A change in bowel habits, manifested by either constipation or diarrhea, or rectal bleeding makes mandatory a digital examination of the rectum. These are the early findings and it is at this stage that the case should be discovered if treatment is to be of any avail. Because of the disturbance of the storage function of the rectum as a result of the growth, constipation and diarrhea are present more frequently than any other symptoms. Lahey[25] stresses the importance of doing a rectal examination on patients with external hemorrhoids, since a fair percentage are associated with rectal carcinoma. Late symptoms are those of weight loss, weakness, anemia, feeling of a weight in the pelvis, and tenesmus.

The diagnosis of carcinoma of the large intestine depends on the history, physical examination, digital examination, X-ray and fluoroscopy, proctoscopy and sigmoidoscopy. Since 70–75% of the cases occur in that portion of the bowel accessable to the sigmoidoscope, these can be diagnosed readily by direct visualization or by biopsy. In those cases occurring higher in the intestine, X-ray with barium and air contrast is of great value in localizing the lesion.

The treatment of all intestinal cancers is surgical removal and either primary resection of the bowel or colostomy followed by resection.

SUMMARY AND CONCLUSIONS

1. Malignant tumors of the small and large intestine are discussed with a review of 76 cases of sarcoma and 142 cases of carcinoma occurring in young people below twenty years of age.

2. Sarcoma of the intestinal tract is most common in the ileum with 59 of the 76 cases localized in this portion of the bowel. Lymphosarcoma is the most common pathologic type, being found in 93.4%.

3. There were 17 cases in the 0–5 age group, 11 in the 6–10 group, 7 in the 11–15 group and 3 in the 16–18 group. Of the cases in which sex was specified, the males predominated 4:1.

4. Illness, wasting, pallor, vomiting, or occult blood in the stools occurring in a child without obvious cause, should suggest sarcoma of the intestine.

5. The course of the disease in the young is rapidly fatal unless suspected and diagnosed early.

6. Carcinoma of the intestinal tract occurs with the greatest frequency in the large intestine. 130 of the 142 cases in this review or 91.5% occurred in the colon and rectum. From the descending colon to the rectum is the most vulnerable area, constituting 73.8% of the cases.

7. 79 cases occurred in the 11–15 age group; males were afflicted twice as often as females.

8. The possibility of intestinal cancer should be at least borne in mind as a diagnostic consideration even in the young age group.

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TUBERCULOSIS PERITONITIS

Case No. 97

Allan B. Coleman, M.D.
Ralph S. Carbo, Jr., M.D. L.D. 45-6373

A twenty-six month old colored male was admitted to the Children's Hospital because of swelling of the abdomen and loose, foul smelling stools, of a month's duration.

The child was born at home in a nearby state; the birth weight and early feeding history are unknown. The mother died of pulmonary tuberculosis when the patient was twenty months of age, and he was subsequently cared for by an aunt. Dietary history revealed inadequacy of vitamin supplements and protein foods. Details of early development were not available. There had been no previous illnesses or operations. A month before admission enlargement of the abdomen was first noted. There was fever for a few days attributed to teething and thrush. From the onset of symptoms there was progressive but intermittent swelling of the abdomen and progressive wasting of the extremities. The stools which had not been notably abnormal, became large, light-colored, and foul smelling during this same period of time.

Physical examination at the time of admission revealed an emaciated, lethargic infant with protuberant abdomen (fig. 1). The rectal temperature was 99 degrees F., pulse 110 and respirations 23. The weight was 21 pounds and height 35 inches. The tonsils were slightly enlarged; small, shotty posterior cervical, axillary and inguinal lymph nodes were palpable. There was moderate beading of the costo-chondial junctions, and flaring of the lower ribs. No abnormalities of the heart or lungs were noted. The abdomen was large and tense, with bulging flanks; no definite evidence of free abdominal fluid was elicited. There was a poorly defined lower abdominal mass, also palpable rectally. The extremities were thin and wasted.

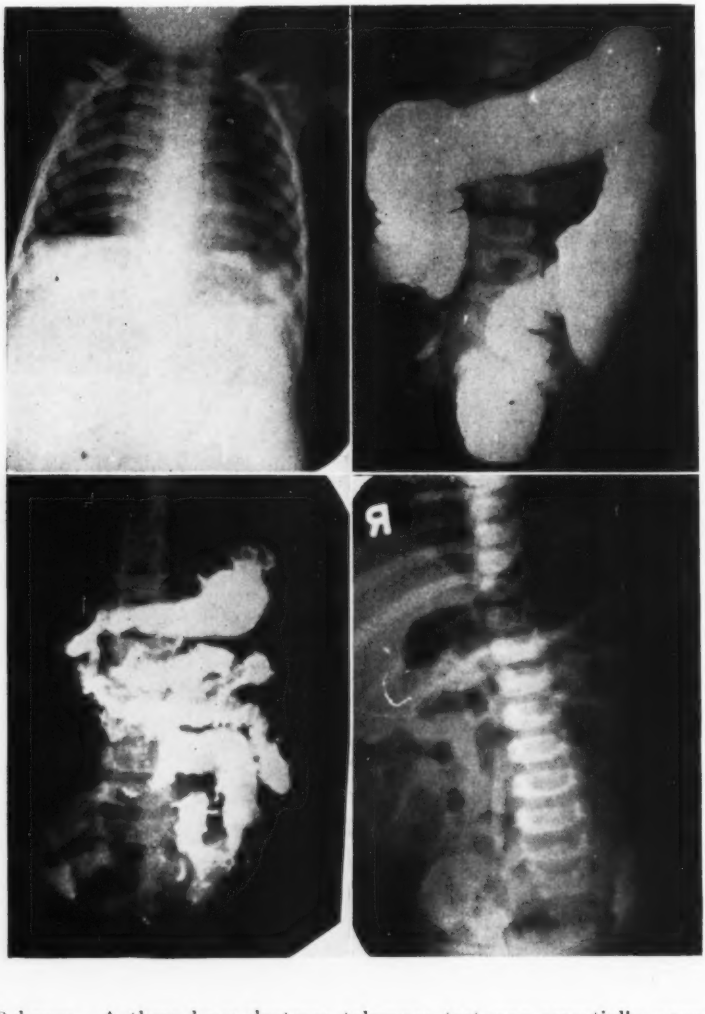
Laboratory examination of the blood showed a hemoglobin of 7.5 gms. % with 3,240,000 erythrocytes, and 10,600 leucocytes of which 54% were lymphocytes, 44% segmented neutrophiles, 2% stab forms and 1% metamyelocytes. The urinalysis was negative. X-ray examination (fig. 2) of the chest revealed a small area of infiltration in the second right anterior interspace, and suggestive evidence of enlarged mediastinal lymph nodes. An intravenous pyelogram and barium studies of the gastro-intestinal tract were negative, except for some abnormality of the small bowel mucosal pattern, and suggestive evidence of displacement of the colon by an extrinsic

abdominal mass. X-ray studies of the long bones were negative. A Mantoux test with second strength purified protein derivative was positive.

FIG. 1—Plate 1, left, Plate 2, right. L.D. at time of admission to the hospital showing markedly distended abdomen and marasmus.

Further studies revealed a sedimentation rate (Wintrobe) of 37 mm. per hour, prothrombin 50% of normal, serum calcium 8 mg. %, phosphorous

4 mg. %, phosphatase (acid) 3 King-Armstrong units, and blood cholesterol 165 mg. %. A cephalin-cholesterol flocculation test was negative after



48 hours. A three hour dextrose tolerance test was essentially normal. Repeated stool examination were negative for ova and parasites and for

excessive amounts of fats and carbohydrates. Three concentrated gastric washings were negative for acid-fast bacilli.

The hospital course was febrile, temperatures ranging from 98 to 104 degrees F., with a tendency toward regular diurnal variations during the latter part of the hospital stay. There was progressive weight loss despite high caloric feedings and large vitamin supplements. The anemia failed to respond to multiple blood transfusions. The stools were large, greenish to brown, usually soft and foul-smelling. A prolonged course of penicillin and a course of sulfadiazine failed to produce any improvement.

On the 39th hospital day an exploratory laparotomy was performed through a right rectus incision, revealing a mass consisting of small bowels matted by a plastic exudate. The peritoneum was studded with small nodules which, on microscopic section showed typical tubercle formation, with caseation and Langhans' giant cells. The post-operative course was progressively downhill despite supportive measures, and the patient died on the 60th hospital day.

DISCUSSION

Tuberculosis causes 2% of the deaths under the age of 2 years, and 3 to 5% of those occurring under the age of 6 years according to Holt[1]. The case fatality rate for tuberculosis in the pediatric age group is greatest in those patients below the age of 3 years[2]. In one series[3], 10% of the cases of tuberculosis admitted to a pediatric hospital were predominately abdominal. Since the preponderance of children who acquire tuberculosis during the first two years of life do so as the result of exposure to an infected member of the household[1], case-finding is especially important in this group. Mackintosh[5] emphasizes the dangers in allowing small infants to have continued contact with an open case of tuberculosis, following their primary infection.

This patient presented a problem in differential diagnosis, involving consideration of idiopathic megacolon (because of the abdominal mass, enlarged abdomen, and bulky stools), and of coeliac syndrome and related disorders (in view of the abdominal enlargement, wasted limbs, foul, bulky stools and pulmonary lesion). The former, however, was eliminated by barium study of the gastro-intestinal tract. The latter diagnostic consideration required more extensive study, but was finally ruled out by the persistently normal fat and starch content of the stools, normal dextrose tolerance, and normal blood cholesterol level, as evidence of adequate fat and carbohydrate digestion.

The combination of a "soft" pulmonary lesion and a positive Mantoux test in so young a child is strong argument for active tuberculous infection; indeed, Kendig and Hardy[6] believe a positive tuberculin test in an in-

dividual below the age of 3 years to be *prima facie* evidence of active infection. However, demonstrable tuberculous lesions elsewhere in the body are often absent in proven cases of tuberculous peritonitis. Barrow[7] in his series of 67 patients, was able to demonstrate such lesions in only 20%.

Justification for laparotomy in suspected tuberculous peritonitis is primarily, to establish the diagnosis and, especially in older children and adults, to rule out abdominal malignancy in those cases in which a mass is present. Also, it is the feeling of many that laparotomy is the preferred method for evacuating peritoneal effusion, a generally accepted necessity[7] in the treatment of peritoneal tuberculosis.

In the case here presented it would seem likely that the patient acquired his primary infection during the neonatal period, followed by "heavy dose" re-infection from a tuberculous mother.

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PRIMARY ANAPHYLACTOID PURPURA

Case No. 98

Robert B. Sullivan, M.D. J.W.B. 46-7071

We would like to present a case of an unusual bleeding tendency which seems best classified as an anaphylactoid purpura. The patient was a nine year old white boy who entered the hospital on September 19, 1946, because of a generalized urticaria and a recurrence of post-tonsillectomy bleeding.

This boy seemed normal until he was one and a half years old when he fell against a bureau cutting the upper gingo-labial reflection. Bleeding continued almost steadily for two weeks in spite of repeated suturing attempts and cauterization. He recovered spontaneously and seemed perfectly well except that he bruised easily. When two and one-half years old he fell on a cement pavement and bit the anterior portion of his tongue entirely off. His mother picked it up and took the boy to a doctor who sutured the tongue part back in place. For the next two weeks the tongue continued to bleed. Recovery was spontaneous however and the tongue healed well.

During the winter when he was six years old he had for the first time episodes of red, warm, painful swelling of one ankle. There were about five different episodes, each lasting two to three weeks. Both ankles were involved but never at the same time. The pain was so severe that he cried loudly. The swelling was marked and he was unable to be out of bed. During the next winter he had three more similar episodes. One was the most severe of all involving the right ankle with the swelling extending up into the calf. There seemed to be little if any fever during these attacks and the attending physician found no involvement of the heart. Between attacks he was quite well and energetic. During the year preceeding his admission there were no recurrences but he had a severe tonsillitis for four days. Nine months before admission he bruised his right arm from the shoulder to the elbow. This remained swollen and discolored for three to four weeks. Recovery was complete. Several months later he fell receiving a three inch laceration on the lateral surface of the left elbow. This healed in a few days without bleeding unduly. In May of 1946 he was struck quite hard in the right knee by a baseball bat and on the next day the knee was swollen and red. The joint has remained swollen since then and the range of motion is quite limited. In June, 1946, he fell on the stairs receiving a one inch laceration just lateral to the left eye. This healed normally. One month later a cast was applied to the right leg to immobilize the knee, the diagnosis being epiphysitis.

In September, 1946, he was admitted to the hospital for a tonsillectomy and adenoidectomy because the infected tonsils were suspected of influencing the diseased knee. One day before admission a hemorrhage measuring almost one centimeter in diameter occurred spontaneously in the lateral sclera of the right eye. Before the operation blood studies including a complete blood count, bleeding time, coagulation time, prothrombin time and Kahn were normal except for a mild anemia, the red blood count being 3.2 million with 9 grams percent of hemoglobin and there was a lymphocytosis of 41% with an eosinophilia of 7%. After the operation oozing began from the right tonsillar fossa and continued with remissions and exacerbations for the next ten days. A circumcision had been done at the same time but there was no post-operative bleeding. Further studies (bleeding time, venous clotting time, clot retraction time, platelet count, icterus index and tourniquet test) demonstrated no abnormalities. He received transfusions for the first time during this admission. He also received amigen, aminoids, moccasin venom, rutin, ascorbic acid and hykinone. The liver and spleen, which were not palpable on admission, were felt four centimeters below the costal margins after one week's bleeding. At his worst he was cold, waxen, pale, comatose, in oxygen and critically ill. After ten days the bleeding seemed stopped and he was discharged on the sixteenth hospital day. Three days later he was readmitted because of generalized severe urticaria and renewed bleeding from the right tonsillar fossa. On this admission only one transfusion was required. Benadryl and phenobarbital seemed effective in controlling and resolving the urticaria. In six days he was discharged in good condition. Eight months later he had gained over thirty pounds and was said to be in excellent general health. However, he had fallen and fractured his right femur just above the knee where the range of motion was still quite limited. The fracture was said to be healing well.

DISCUSSION

Anaphylactoid purpura (nonthrombocytopenic purpura) is a disease of an unusual bleeding tendency which is thought to be due to abnormal or damaged capillaries. The secondary form is encountered during bacterial endocarditis, meningococcic meningitis, septicemia, pneumonia, pyonephrosis, tuberculosis, glomerulonephritis and in many intoxications. The diagnosis of primary anaphylactoid purpura should be considered when no infection or intoxication can be indicated and no abnormalities of the blood can be demonstrated. The platelet count and the clot retraction time are normal. The bleeding time may be prolonged and the tourniquet test is usually positive but may be negative. Two clinical types are recognized. In Schönlein's purpura one or more joints become red, swollen and tender

simulating rheumatic fever closely. Skin lesions may appear at once or be delayed for days. There may be petechiae, ecchymoses or urticaria. Henoch's purpura is characterized by abdominal pain often with vomiting. Blood may or may not appear in the stools. The abdomen is tense and tender. The skin lesions are similar to those described above. In both types there is usually fever, leucocytosis and eosinophilia.

There is no specific treatment. Transfusion is indicated as determined by the blood count. Toxic substances and allergic factors should be searched for. Vitamin C, moccasin snake venom, parathyroid extract and histamine desensitization have been tried with varying success. Splenectomy is contraindicated. The prognosis is usually good and recovery is spontaneous.

In the case presented here there were three episodes of unusual bleeding and nine instances of red, warm, swollen, tender joints. Ectodermal manifestations included easy bruising, a spontaneous scleral hemorrhage, and generalized urticaria. There was no familial history of a similar disease though the maternal grandmother and a maternal aunt both had a suggestive history of rheumatic fever. The patient's only known allergy was to aspirin. On four or five occasions ingestion of aspirin had caused swelling of the eyes and face but no relation between this idiosyncrasy and his disease could be established. The absence of infection or intoxication and the negative blood study suggests the diagnosis of primary anaphylactoid purpura.

E. COLI PYELONEPHRITIS ASSOCIATED WITH HYDRONEPHROSIS TREATED WITH STREPTOMYCIN

Case Report No. 99

Martin F. Randolph, M.D. T.C. 47-3037

A nine month old white female was admitted to the hospital for the first time on March 27, 1947 with the chief complaint of vomiting and fever.

The infant was born June 14, 1946 of a normal, full term, spontaneous delivery at a local hospital. It was noted at birth that the first to fourth toes inclusive of her left foot were missing; no other abnormalities were noted. The infant's developmental and feeding history were apparently normal. Family history was essentially negative and the father and mother are living and well. There were no siblings. The past history was noncontributory.

The patient had a "cold" for one week preceeding admission. Two days before admission on March 25th, the infant vomited twice and had a temperature of 103° that evening; there was no diarrhea. She was seen by a local physician and no definite diagnosis was made, the patient was given sulfadiazine and oral penicillin therapy without effect. One of our staff members was consulted and the patient was admitted to the hospital for study.

On admission the physical examination revealed an irritable, acutely ill, nine month old white female with the following positive findings: temperature 103°, pharynx and tonsils mildly inflammed and the ears slightly injected; toes one to four inclusive were absent from the left foot.

Admission diagnosis was acute pharyngotonsillitis, bilateral catarrhal otitis media and congenital absence of first to fourth toes, left foot.

The patient was placed on sulfadiazine therapy, forced fluids and a regular diet for her age, which she took fairly well. The hemogram on admission was within normal limits. Repeated urinalyses showed zero to 50 mgm.% of albumin with occassional white and red blood cells; there were no casts reported. A urine culture was taken on the 3rd hospital day and showed non-hemolytic Staphylococcus albus. The urine culture was repeated on the following day and showed 15 colonies of non-hemolytic Staphylococcus albus. Because this organism is such a common contaminant and in view of the low colony count, the culture was not considered as being too significant.

The patient ran a septic course during the first three hospital days and appeared acutely ill. On her third hospital day she was started on penicillin therapy (20,000 units every three hours) and by the following day her

temperature began to fall by lysis, reaching normal on the 7th hospital day. Therapy was discontinued on the 9th day and the patient was discharged 24 hours later, after 3 days of normal temperature. At the time of discharge, the parents were instructed to bring the infant back within three weeks for urinalysis and culture.

The patient was re-admitted to the hospital with the chief complaint of "high fever" on the 12th day of April. The infant had been perfectly well for six days following discharge and became febrile 24 hours before re-entry.

Physical examination on admission revealed an acutely ill, feeble, irritable infant with a temperature of 102°. The only positive findings were a mildly injected pharynx, and congenital absence of first to fourth toes inclusive on the left foot as previously noted.

In view of the findings on the previous admission a recurrent urinary infection was considered likely and because of the presence of one congenital defect, an anomaly of her urinary tract was viewed as a good possibility.

On admission the red blood cell count was 3,700,000 with 10.5 grams of hemoglobin; the white blood count was 17,800 with 60% polymorphonuclears, 38% lymphocytes and 2% monocytes. Urinalysis showed 40 mgm.% of albumin and innumerable white blood cells; the urine culture revealed *E. coli*. A blood culture was negative.

Therapy consisted of sulfathiazole and supportive parenteral fluids. This was continued for three days but no improvement was noted; the temperature remained elevated in spiking fashion. On April 15th, the non-protein nitrogen was 69 mgm.% and the blood urea nitrogen was 47 mgm.%. The urine still showed clumps of white cells but no red blood cells or casts. At this time a large, firm, movable mass could be felt in the left upper quadrant which was considered to be kidney. An intravenous pyelogram was done and the report read as follows: "Examination of the genito-urinary tract at the end of 4 minutes reveals the presence of some large clumps of opaque material on the right and at the end of 10 minutes they are visualized as greatly dilated and enlarged calices; at the end of 20 minutes a greatly dilated pelvis on the right is visualized and there is still nothing seen on the left; at the end of 30 minutes there is very little dye in the bladder indicative of greatly impaired function and the left kidney is not visualized at any time." Roentgenologically, the interpretation was that of an advanced bilateral hydronephrosis.

Streptomycin, 150,000 units every three hours intramuscularly, was begun the 15th of April and sulfathiazole therapy simultaneously discontinued. With streptomycin therapy there was an almost immediate improvement in the patient's clinical status and a sharp fall in temperature to normal within 12 hours. Urine culture taken 24 hours later was negative and cleared remarkably showing only a few white blood cells and a few

red blood cells. Her improved clinical state continued and temperature remained normal for approximately 56 hours when, still on streptomycin therapy, it rose to 101° on April 18th and rose again to 100° on April 19th. At this time urinalysis again showed small clumps of white blood cells and the urine culture was positive for non-hemolytic *E. coli*. Non-protein nitrogen at this time was 47 mgm.%. The patient began vomiting, became feeble, apathetic and refused her feeding.

Meanwhile, a retrograde pyelogram done on 5th hospital day corroborated the findings of the intravenous pyelogram, viz. a marked hydronephrosis and hydroureter on the right side. The left side could not be catheterized.

It became apparent that the patient's *E. coli* infection was not responding to the dosage of streptomycin administered. Accordingly, it was decided to discontinue streptomycin therapy and run streptomycin sensitivity tests on the E. coli organism cultured from the patient's urine. Streptomycin was discontinued on the 10th hospital day and twenty-four hours later the temperature rose to 104° and the urine showed a great many white blood cells in clumps and many bacteria. Urine culture again grew out hemolytic E. coli and streptomycin sensitivity tests done after the method of Prince, Nielson and Welch (6) revealed the organism to be sensitive to .5 units and 1.5 units of streptomycin in two different cultures. We were encouraged by the low sensitivity of the organism and felt that the apparently poor response to streptomycin therapy was due to the obstruction and stasis in the genito-urinary tract.

On the 12th hospital day a second intravenous pyelogram was done which visualized both kidneys as greatly enlarged with large clumps of radio-opaque material in the calyces. At 20 minutes there was still no dye visualized in the bladder. At the end of 3 hours, large dilated calyces, pelvis and ureters were observed; the bladder was well outlined and normal in size, shape and position. It was necessary to wait 3 hours before the left kidney could be visualized. This represented a confirmation of the original roentgenological impression of hydronephrosis and hydroureter with probably less than one per cent function remaining.

On April 25th, the 13th hospital day, the patient developed a diarrhea of loose yellow and brown stools without mucus or blood. She was given streptomycin 100,000 units every 3 hours orally and the diarrhea largely subsided in 48 hours. Streptomycin was discontinued April 29th, 24 hours before death.

Her condition in the last seven hospital days was one of severe toxicity. Vomiting was frequent and she was sustained on parenteral fluids, plasma and blood transfusions. Her temperature remained persistently elevated. The blood pressure at this time was 135/80. The urine continued to show

a great many white blood cells and red blood cells began to appear in large numbers. Non-protein nitrogen two days before death was within normal limits. The patient expired on April 30th, her 18th hospital day.

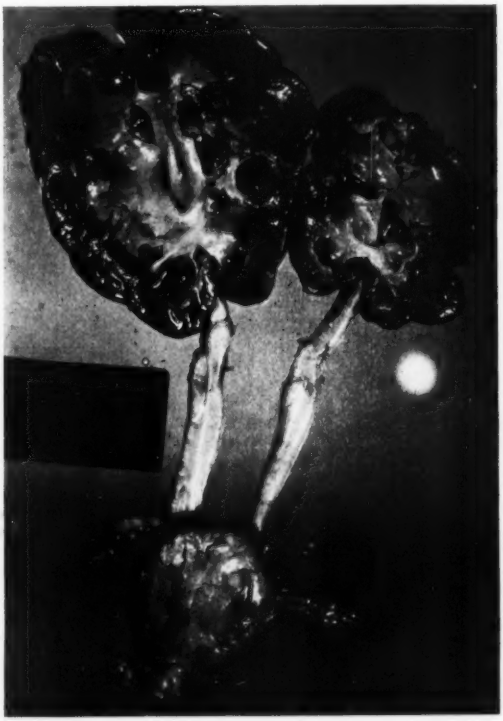

FIG. 1

AUTOPSY FINDINGS

E. Clarence Rice, M.D.
Frank Murphy, M.D.

The left kidney was markedly enlarged weighing approximately five times normal. The right kidney was enlarged to a lesser degree. Cut section of the kidneys showed the cortices to be markedly thinned, the pelves and calyces being greatly dilated. Both ureters were dilated throughout their course to a circumference of one and a half centimeters. By means of a syringe of water, non obstructed paths could be demonstrated

from both pelves through the ureters, the bladder and the urethra. Upon opening these structures there were no valves or mechanical obstruction demonstrable. There was some hypertrophy of the ureteral walls. The bladder was small and slightly hypertrophied while the urethra appeared normal (figures 1 and 2).

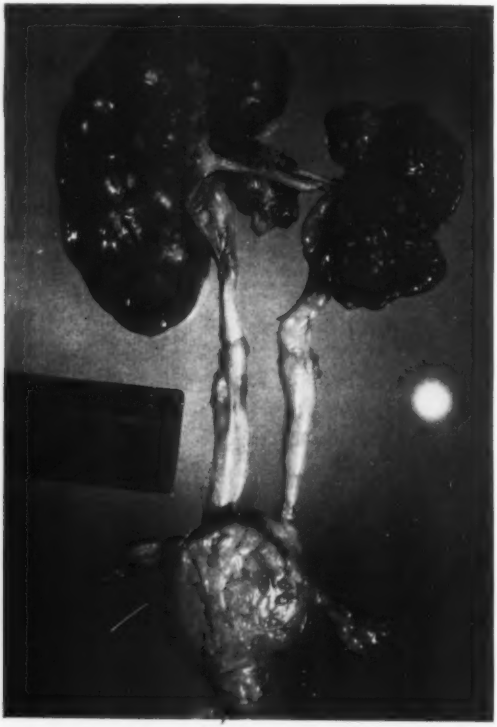

FIG. 2

Microscopic examination revealed the glomerular capillaries to be distended with blood and some glomeruli showed moderate capsular thickening. The interstitial tissue contained large numbers of polymorphonuclear leucocytes and some round cells with atrophy of the tubules. In the medullary region all of the tubules were dilated and filled with polymorphonuclear leucocytes and there was flattening of the epithelial cells.

Cultures made at necropsy revealed non-hemolytic Staphylococcus albus present in the heart's blood and in both kidney pelves while the latter also showed Escherichia coli.

There was an associated chronic myocarditis with evidence of cardiac failure, there being pulmonary edema, pleural, pericardial and peritoneal effusions.

Syndactyly of the left foot was also noted.

ANATOMICAL DIAGNOSES:

1. Chronic myocarditis.
2. Pulmonary edema.
3. Pleural and peritoneal effusions.
4. Bilateral hydronephrosis and hydroureters.
5. Bilateral pyelonephritis and chronic ureteritis.
6. Syndactyly of the left foot.

DISCUSSION

Martin F. Randolph, M.D.

The use of streptomycin in the control of genito-urinary infections when abnormal renal function exists poses the problem of erratic levels of the drug in the urine and the great danger of the organism becoming resistant. Such was the problem in the case just presented.

Recent work done on the use of streptomycin in gram negative infections of the genito-urinary tract (1, 2) indicate this antibiotic to be the drug of choice. But the initial dose must be high, the dosage sustained at adequate levels in the urine and the infection brought under control rapidly. To meet these objectives, the sensitivity of the infecting organism must be known, the over-all streptomycin level in the urine must be known and the focus that is feeding the infection to the urinary tract must be controlled.

Knop has demonstrated the ease and rapidity with which bacteria develop increasing resistance to streptomycin. Working with bacteria commonly found in urinary infections, Knop found strains of E. coli to be initially inhibited at 3.1 to 12.5 units of streptomycin per cc. of media. After only seven to twelve serial transfers to media containing gradually increasing amounts of streptomycin these same strains were made resistant to 1000 units of streptomycin. Other organisms (Streptococcus fecalis, Aerobacter aerogenes, etc) subjected to the same in vitro methods developed a similar resistance.

This faculty of the development of resistance makes imperative the maintenance of uniform adequate levels of this antibiotic in the urine. Much has been written on the absorption and excretion of streptomycin (3, 4). These studies showed levels in the urine two to four hours after the parenteral administration that are more than adequate to deal with any gram negative infection (2). But the data given apply only in the presence of normal renal function. When kidney excretion is irregular the only way to

determine that streptomycine levels are uniformly adequate is to make frequent quantitative estimates of the drug in the urine.

There is a possibility that when treating a genito-urinary infection that has as its infectious agent an organism common to the flora of the gastro-intestinal tract, that streptomycin may be used with profit both orally and parenterally. With the use of oral streptomycin the intestinal flora can be reduced considerably thus quantitatively lessening the source that is infecting the genito-urinary tract.

In the case presented above, the prognosis was nil. Still, in an academic way, and for future reference, we feel that her infection could have been more efficiently controlled if streptomycin were given by mouth, if follow-up streptomycin sensitivities were done on the responsible organism, if periodic streptomycin levels were done on the urine and the parenteral dose adjusted accordingly.

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